GALENICAL COMPOSITIONS

This is a continuation-in-part of our co-pending application Ser. No. 208,181, filed Nov. 19th, 1980, now abandoned which in turn in a continuation-in-part of our application Ser. No. 82,487, filed Oct. 9th, 1979, now abandoned, which in turn was a continuation of our application Ser. No. 16,950, filed Mar. 2nd, 1979, now abandoned.

This invention relates to galenical compositions, particularly compositions containing a pharmacologically active mono-cyclic peptide.

Because of the hydrophobic and/or lipophilic character of such peptides, pharmaceutical formulations thereof with conventional solid or liquid pharmaceutical excipients tend to have disadvantages. For example the peptide may not be satisfactorily absorbed, the composition may not be well tolerated, the composition may not be sufficiently stable on storage, e.g. against crystallizing-out of the peptide, and/or the concentration of the peptide capable of being solubilized without crystallizing-out may be low, e.g. of the order of 3% or lower.

Problems of this nature arise not only with liquid formulations, but such solid forms such as solid "solutions", e.g. in the form of oral pellets, produced for example by melting a solid carrier, mixing in the active ingredients and allowing the mixture to solidify.

While there are many known proposals to alleviate or overcome problems of this type, it has been found after exhaustive trials that many of these proposals are inadequate in the area of the monocyclic peptides, in particular cyclosporins, with which the invention is concerned. It has, however, surprisingly been found that certain classes of glycerides used as carrier components do assist in alleviating these difficulties; in particular they, for example, may enable achievement of higher blood levels of active agent or avoid other problems such as instability.

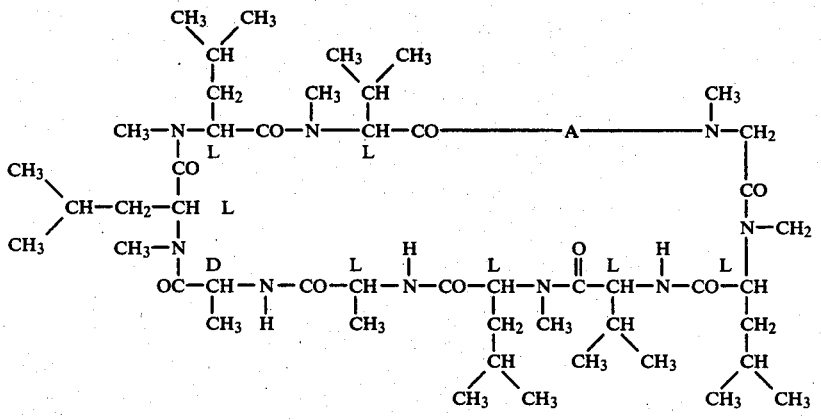
The present invention accordingly provides a pharmaceutical composition comprising a pharmacologically active mono-cyclic peptide and carrier comprising at least one of the following components:

(a) a trans esterification product of a natural or hydrogenated vegetable oil triglyceride and a polyalkylene polyol,

(b) a saturated fatty acid triglyceride, and

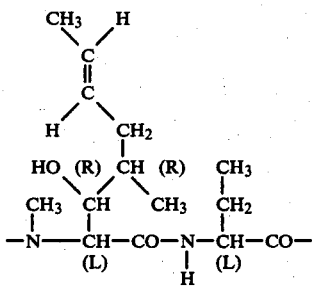
(c) a mono- or di-glyceride.

The compositions of the invention are particularly suitable for hydrophobic and/or lipophilic peptides which are insoluble or difficultly soluble in conventional pharmaceutical vehicles, in particular cyclosporins, including those having a basic ring structure as follows:

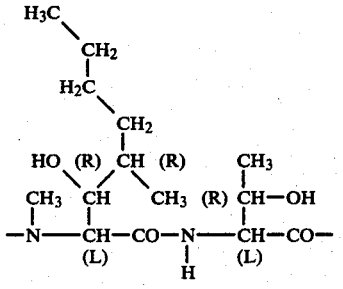


wherein A is a bivalent moiety containing two amino acids linked together.

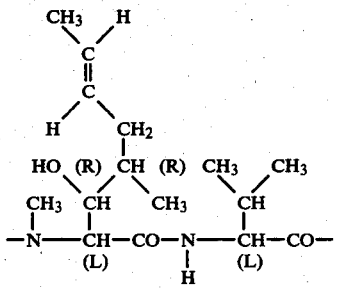
A may be for example:



(cyclosporin A)



(dihydro-cyclosporin C)



(cyclosporin D)